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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/812,991	03/04/97	NESTOR J	28200-C3

NM11/1215

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EXAMINER	
BERCH, M	

ART UNIT	PAPER NUMBER
1611	

DATE MAILED: 12/15/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/812,991	Applicant(s) Nestor
	Examiner Mark L. Berch	Group Art Unit 1611

☒ Responsive to communication(s) filed on *11/9/98* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *23-28* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *23-28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for CMV, does not reasonably provide enablement for treating herpesviruses generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons were given previously; the traverse on this point is unpersuasive.

Applicants argue that the examiner has not presented evidence that one of ordinary skill in the art would "reasonably doubt the asserted utility." The examiner has done exactly that. Despite vast amounts of research into treating herpesviruses, no antiviral has ever been effective in treating herpesviruses generally. In view of the marked differences among the herpesviruses, this failure is reasonable evidence that the skill level in this art is not sufficient for such a task, and indeed may be inherently impossible. The examiner has particularly pointed to EBV, a virus linked to a number of serious illnesses. No one has been able to get antivirals effective against e.g. HSV-1 to be effective against EBV. Furthermore, as noted previously, the claimed

compound is a prodrug of Ganciclovir. Thus, it would reasonably be presumed to be ineffective against what Ganciclovir is ineffective against, viz, EBV or HHV-8. It would be pretty much unprecedented for a prodrug of a known antiviral to be effective against a much broader range of viruses than the parent compound is. The examiner is aware of the fact that the specification states that Ganciclovir is effective against e.g . EBV. However, as a practical matter, this simply is not true. Ganciclovir is not effective against IM, Burkitts lymphoma or any other disorder which is caused by EBV. If applicants actually wish to argue that Ganciclovir is effective against diseases caused by EBV or HHV-8, etc, they are invited to present evidence to that effect.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 23-28 are rejected, 35 U.S.C. 102(b) as anticipated by Beauchamp.

The reasons were given previously; the traverse on this point is unpersuasive. An impasse has clearly been reached on this issue. This issue appears in the parent 08/453223 as well.

Claim Rejections - 35 USC § 103

Claims 23-28 are rejected, 35 U.S.C. 103 as obvious from Beauchamp.

The generic formula embraces the claimed compounds. A prodrug form, the valinate, appears in example 5. The sole difference is that example 5 is the bis ester,

whereas the claims are drawn to the monoester. However, the generic formula covers only two forms: the monoester and the diester, and hence such a variation is obvious. Monoesters are recognized as a specific group at column 2, line 26. It is agreed that the bis is preferred over the monoester. However, a reference is available for all that it teaches, not just the best or even the preferred embodiments. In this regard, see *In re Lamberti*, 192 USPQ 278, 280; *In re Boe,* 148 USPQ 507, 510; *In re Fracalossi*, 215 USPQ 569, 570.

The fact that a different monoester was produced as what applicants call an "incidental impurity" does not detract from the explicit teaching of the reference. And the argument is that it "is obvious because it would be desirable" misses the point. It is obvious because that is what the reference explicitly teaches.

Claims 23-28 are rejected as obvious, 35 U.S.C. 103 from Verheyden in view of Beauchamp (1992).

The reasons were given previously; the traverse on this point is unpersuasive.

Applicants point out that Verheiden has no teaching of Ganciclovir esters, but the reference is not being used alone; it is used in combination with Beauchamp (1992), which supplies just that deficiency.

Applicants point out that esterification of Ganciclovir, without special blocking procedures, will produce the bisester, or its mixture with the monoester. But these are not manufacture claims. If the monoester is obvious, one of ordinary skill in the art will know how to make it.

Applicants point out that Acyclovir is a monoester because there is only one OH. It is true that Acyclovir can form only a monoester. It is not seen how that removes its teaching of forming a monoester just because it cannot form a bis, tris or tetrakis ester.

Applicants state, "the Examiner's reasoning would say that inflating a tire..." The examiner never raised the analogy of inflating a tire.

Applicants state that Beauchamp (1992) "suggests the desirability of Acyclovir monovalinate, not of valinates of nucleosides." It does more than "suggest", that is the explicit teaching. Further, the examiner does not need to generalize all the way to "nucleoside", only to Ganciclovir, which is of such close structure that one skilled in the art of antivirals would logically apply it to Ganciclovir as well.

Applicants state that "a fair reading of Verheiden in view of Beauchamp (1992) would suggest only bis-esterification." How does applicant arrive at "only bis-esterification" from a reference which teaches only mono-esterification?

Applicants have presented a Malcolm declaration. This includes an explanation of sorts of why the results are at such sharp variance with the data in the specification. However, why is this data different from the data presented previously in the "Memorandum of Record" submitted with the Reply Brief submitted in the parent? Three out of the five reported numbers are different, and all the Standard Deviations are different.

Further, the data shows expected, not unexpected differences. Acyclovir monovalinate has 53.4% bioavailability; the corresponding claimed Ganciclovir monovalinate has 55.4%. Given the fact that the exact numbers that are obtained are a rather sensitive function of the exact details as to how the test is run (as declarant sets forth in paragraph 9), such a difference is hardly meaningful. Preparing the Acyclovir valinate puts it into a form where about half is bioavailable; the same has now been found true for the claimed Ganciclovir monovalinate. One would expect from the Acyclovir results just what was actually found, and hence no unexpected results are seen. The declarant notes the 1.6 ratio between the Ganciclovir mon and di-esters of Ganciclovir (up from the 1.5 ratio seen in the previously presented "Memorandum of Record") However, as the examiner has repeatedly pointed out, the rejection is not over the bisvalinate. Hence, comparison with the bisvalinate does not establish patentability in this rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 51-56 of copending Application No. 08/453223. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no patentable distinction.

The claims in the parent are drawn to the crystalline form. Here, the claims are slightly broader, covering both crystalline and non-crystalline. A claim which covers two forms will clearly render obvious a claim which recites just one. And a claim which covers one form anticipates a claim which is generic to it, covering both.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718.

Mark L. Berch

Primary Examiner

Group 1610 - Art Unit 1611

December 11, 1998